Prenatal diagnosis of atypical adrenal neuroblastoma with pulmonary metastases is possible: Impact on the assessment of prenatal prognosis

N. Menager a,b, E. Quarello b,c,d, M. Capelle a,b, V. Lacroze b,e, C. Coze f, P. De Lagausie b,g, G. Gorincour b,h,*

a Department of Gynecology and Obstetrics, hôpital La Conception, 147, boulevard Baille, 13385 Marseille cedex 5, France
b Multidisciplinary Center for Prenatal Diagnosis, Children’s Hospital La Timone, 264, rue Saint-Pierre, 13385 Marseille cedex 5, France
c Obstetric ultrasound unit, pôle Parents-enfants, hôpital Saint-Joseph—Marseille, 26, boulevard de Louvain, 13285 Marseille cedex 08, France
d The Medicine Institute of Reproduction, 6, rue Rocca, 13008 Marseille, France
e Department of Neonatology, hôpital La Conception, 147, boulevard Baille, 13385 Marseille cedex 5, France
f Department of Paediatric Oncology, Children’s Hospital La Timone, 264, rue Saint-Pierre, 13385 Marseille cedex 5, France
g Department of Pediatric Surgery, Children’s Hospital La Timone, 264, rue Saint-Pierre, 13385 Marseille cedex 5, France
h Department of Pediatric Imaging, Children’s Hospital La Timone, 264, rue Saint-Pierre, 13385 Marseille cedex 5, France

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A 24-year-old woman was referred at 35 weeks’ gestation, after ultrasound diagnosis of a fetal tumour near the kidney. Ultrasound showed a 6 cm tissular mass, heterogeneous and hypervascular, developed from the upper pole of the left kidney or adrenal gland (Fig. 1a). The diagnoses discussed were neuroblastoma (NB), adrenal hematoma, kidney tumour, and subdiaphragmatic bronchopulmonary sequestration. Magnetic resonance imaging (MRI) confirmed the tissular nature and exorenal location, coinciding with the midline and displacing retroperitoneal vessels (Fig. 1b). Its signal was heterogeneous, hyperintense in T2. No other lesion was found. The patient was informed of the likely adrenal origin and the difficulty of exclusionary formal differential diagnoses before birth. Ultrasound at 37 weeks’ gestation found a slight increase in size. Moreover, a polyhydramnios appeared with cardiomegaly, dilated right atrium and a slight tricuspid regurgitation (60 cm/sec), an increase of maximum velocity of the middle cerebral artery (Vmax MCA)
corresponding to 1.74 MoM. Anaemia due to bleeding, haemolysis within the tumour or high cardiac output failure could explain these signs. Amniodrainage was decided because of dyspnea and poor maternal hemodynamic tolerance, then a caesarean section was decided. A 3,060-g girl was born. Her status deteriorated rapidly. She was intubated and transfused, given a 12 g/dL moderate anaemia. Urinary catecholamines were significantly increased, noradrenalin particularly. A thoracic and abdominopelvic computed tomography (CT) scan carried out at 24 hours of life found a 7.7 cm left retroperitoneal tissular lesion, characterized by a spontaneous hypodensity with some punctuate calcifications, enhancing heterogeneously with contrast media and without macro-systemic vascularisation. There was a fatty peripheral cleavage plane with the aorta, and a 26 mm tissular mass on the contralateral adrenal gland which was not seen on prenatal imaging and had probably increased since then. In the liver was a hypodense macronodular formation; its metastatic nature was supported by targeted ultrasound showing multiple hyperechoic liver nodules, revealing Pepper Syndrome. In addition, thoracic CT showed several intrapulmonary nodular formations (Fig. 1c) also suggesting metastases. Looking back at the fetal MRI, it was clear that at least one pulmonary metastasis was present (Fig. 1d), but no liver metastases could be retrospectively visualized. A meta-iodobenzylguanidine scintography (MIBG) uptake test showed a right adrenal region and left hepatic uniform fixation, reinforcing the external part of the left lung, and a very suspicious skull mass. A surgical “debulking” to minimise the tumour and try to control hemodynamics was performed. A laparotomy enabled resection of a retroperitoneal encapsulated intra-adrenal tumour weighing 192 g. It was a poorly differentiated NB with unfavourable mitotic index. A myelogram performed on a tibial crest also showed metastatic invasion. Placenta did not show metastasis. In summary, it was an adrenal secreting NB stage IV according to the International Neuroblastoma Staging System (INSS). The patient then received two courses of chemotherapy. A whole body
MRI control at 4 months showed an absence of signal abnormality in the right adrenal area, and a stable left adrenal lesion. There was a regression of the left parietal lesion in the number and size of the hepatic lesions, and the left basal pulmonary lesion had disappeared. Two new courses of chemotherapy are planned.

NB is a tumor arising from the sympathetic embryonic tissue. It is the most common solid cancer of early childhood. About 93% of NBs are located at the adrenal gland. Prenatal diagnosis of adrenal NB takes place often after 32 weeks’ gestation, although it has been described as early as 22 weeks. It is classically right suprarenal (60%), appears cystic in 50% of cases if not solid or mixed. Calcifications are less common than in the pediatric population where they are classic [1]. Differential sonographic diagnoses of the suprarenal NB, whether tissular, cystic, or mixed, are adrenal haemorrhage, extralobar subdiaphragmatic pulmonary sequestration (ESPS), mesoblastic nephroma and adrenal carcinoma. Only 50% of suprarenal masses are NB. One must therefore be cautious when establishing this diagnosis [2]. Many elements of our observation favoured ESPS. Classically on the left (90%), it is almost exclusively tissular. In our case, there was no arterial supply from the aorta, but the tumour was highly vascular, which is not typical of NB. The systemic vasculature of an ESPS can be underdiagnosed with ultrasound and prenatal MRI [3]. ESPS can be classically complicated with hemodynamic failure, which could explain the discrepancy between moderate anemia and severe hemodynamic failure, which was actually caused by a massive tumoral secretion of catecholamines. Finally, classical forms of ESPS change little in size, while NB can grow rapidly, which allows for its diagnosis in the third trimester [4]. In our case, the increase in size was small and not very discriminative. In order to precise the diagnosis, a test for homovanillic acid in the amniotic fluid could be carried out. However, a literature review by Acharya et al. of 55 cases showed that about 65% of diagnosed prenatal NB are non-secretant [5]. This method seems nevertheless underutilised, as the assay appears to be specific [6]. Invasive sampling will therefore be performed if its result influences monitoring or taking further action.

Once the diagnosis is strongly suspected, one must know how to use all the tools to refine the prognostic evaluation. Indeed, prognosis is very variable, and guided by several criteria. Cystic appearance is associated with a histological appearance consistent with involution: small aggregates of neuroblasts in the cyst wall (suggestive of in situ NB), rather than sheets of tumour cells (encountered with invasive NB). Actually, these cystic NBs often have favourable biological markers and are less often secretant [1]. It appears therefore that the cystic nature of the tumour may be a favourable prognostic factor. Postnatal monitoring strategies are proposed at birth with a non-negligible probability of spontaneous regression, especially for asymptomatic cystic NB, with a good prognosis without biological and remote extension [7,8]. Surgical indications can certainly be considered if size increase occurs. The stage of the INSS classification seems to be the major prognosis factor. The preferred metastatic site is the liver (approximately 25% of patients according to Acharya), but it has been shown that prenatal ultrasound detection is difficult and can perhaps be caught by fetal MRI [5].

Other metastatic sites are possible, such as skin or bones. MRI performed at 35 weeks’ gestation, after analysis of postnatal CT scan, indicates that at least one pulmonary metastasis was visible, which had not yet been described in the literature; we must therefore search for it more specifically in the future. One may also develop dedicated MRI sequences for bone metastases or propose a fetal CT scan.

Our case demonstrates the need to closely monitor suspected antenatal NB, the maximum interval between two ultrasound examinations should not exceed 2 weeks. Prenatal diagnosis of NB and its extent allows to plan the birth appropriately and to better inform the future parents. Prenatal diagnosis is playing an increasing role, so the challenge is now to distinguish between localised and disseminated forms. MRI helps to optimise discrimination and can be used not only to examine hepatic metastases, but also lungs and bones.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References